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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/611,419	07/06/2000	Leonard A. Smith	067252.0105	6819

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 10/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/611,419	SMITH ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-51,53,55,56,82 and 85-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *87* is/are allowed.

6)☒ Claim(s) *42-51,53,55,56,82,85,86 and 88-92* is/are rejected.

7)☒ Claim(s) *43-47,49-51,53,55-56,88-92* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 42-51,53, 55-56, 82, 85-86 and 87-92 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. (***Claim Objections Withdrawn***) Claims 50-51 and 55-56 objected to because of the following informalities have been obviated by amended of the claims to define the organism to be a host cell and by deleting the second recitation of the term "claim".

3. ***(Claim Rejections - 35 USC § 112, second paragraph, Withdrawn)*** Claim 49 no longer recites the limitation "recovering from said transfected cell at least one insoluble polypeptide" thus obviating the rejection.

1. ***(Claim Rejections - 35 USC § 112, second paragraph, withdrawn)*** Claims 50 and 51 rejected for reciting the phrase "wherein said organism" has been obviated by amendment of the claims to recite the term "host cell".

2. ***(Claim Rejections - 35 USC § 112, second paragraph, withdrawn)*** Claim 53 rejected for reciting the phrase "isolating from said transfected cell at least one insoluble polypeptide has been obviated through removal of the term "insoluble" form the claim.

3. ***(Claim Rejections - 35 USC § 112, second paragraph, withdrawn)*** Claims 55-56 rejected for reciting the limitation "the AT content" has been obviated through amendment of the claim to recite the phrase "said nucleic acid has an overall AT content.

4. ***(Claim Rejections - 35 USC § 112, second paragraph, withdrawn)*** Claims 85-86 rejected for reciting the limitation "said polypeptide is at least 0.75% (w/w) of the total cellular protein" or" said polypeptide is at least 20.0% (w/w) of the total cellular protein has been obviated through amendment of the claims limitations to require expression of the encoded polypeptide.

Allowable Subject Matter

5. Claim 87 defines over the prior art of record and is therefore allowed.

Response to Arguments

6. Applicant's arguments filed August 4, 2005 have been fully considered but they are not persuasive.

7. ***(Claim Rejections - 35 USC § 102, Rejection Maintained)*** Claims 42-44, 45-47, and 82 rejected under 35 U.S.C. 102(b) as being anticipated by Kurazono et al (July 1992) as evidenced by Dertzbaugh et al, and Binz et al sequence Swiss Prot accession number P10845 is traversed

on the grounds that SEQ ID NO 3 which encodes SEQ ID NO 4 are not disclosed nor described by Kurazono et al, and Exhibits A and B have been submitted to show that the nucleic acid of Kurazono et al does not share 100% sequence identity with the claimed nucleic acid sequences.

1. It is the position of the examiner that based upon the definitions provided in the instant Specification and what is now claimed, the claimed invention includes nucleic acid molecules that encode peptide fragments of SEQ ID No 4, that include at least one epitope and need not share 100% sequence identity over the entire SEQ Id NO 3 sequence, but need only encode least one epitope within the sequence of SEQ ID NO 3 that encodes an amino acid sequence of SEQ ID NO 4. Dertzbaugh et al provides evidence that the nucleic acid sequence of Kurazono et al (July 1992) encodes at least one epitope of SEQ ID NO 3. Kurazono et al still anticipates the instantly claimed invention.

2. The scope of what is now claimed includes portions of SEQ Id NO 3 which encodes portions of SEQ ID NO 4 based upon the claim language recited "said amino acid sequence comprising at least one immunogenic epitope" and the definitions provided in the instant Specification. See instant Specification "a nucleic acid sequence selected from (page 7, lines 7-8)"; "selecting at least a portion of the codons encoding HC from codons preferred from expression in a host organism (page 7, lines 29-31)"; "fragments of the botulinum neurotoxin protein expressed by recombinant organisms. Specifically peptides comprising protective epitopes from the receptor binding domain(see page 11, lines 23-24); "The vaccine comprises fragments of the A and B toxins (page 11, lines 31-32)"; to include peptide epitopes and not the complete amino acid sequence of SEQ Id NO 4, wherein the claims are directed to a nucleic acid that encodes at least one epitope. The alignment provided is not commensurate in scope with

the instantly claimed invention. The rejection could be obviated by amending the claims to no longer recite [at least one epitope] and just to recite " comprises... SEQ ID NO 3." The rejection is maintained for reasons of record.

8. ***(Claim Rejections - 35 USC § 102, Rejection Maintained)*** Claims 42-50, 53, 82 and new claims 88-92 rejected under 35 U.S.C. 102(b) as being anticipated by LaPenotiere et al (May 11-13, 1992, disclosure presented at the International Conference on Botulinum, Tetanus, Neurotoxins: Neurotransmission and Biomedical Aspects, Madison, Wisconsin) as evidenced by the New England Biolabs product description of pMal (see LaPenotiere et al, page 464, paragraph 2, line 2) P10845 is traversed on the grounds that SEQ ID NO 3 which encodes SEQ ID NO 4 are not disclosed nor described by LaPenotiere et al , and Exhibits A and C have been submitted to show that the nucleic acid of LaPenotiere et al does not share 100% sequence identity with the claimed nucleic acid sequences.

3. It is the position of the examiner that based upon the definitions provided in the instant Specification and what is now claimed, the claimed invention includes nucleic acid molecules that encode peptide fragments of SEQ ID No 4, that include at least one epitope and need not share 100% sequence identity over the entire SEQ Id NO 3 sequence, but need only encode least one epitope within the sequence of SEQ ID NO 3 that encodes an amino acid sequence of SEQ ID NO 4. The nucleic acid sequence of LaPenotiere et al encodes at least one epitope of SEQ ID NO 3. LaPenotiere et al still anticipates the instantly claimed invention.

4. The scope of what is now claimed includes portions of SEQ Id NO 3 which encodes portions of SEQ ID NO 4 based upon the claim language recited "said amino acid sequence

comprising at least one immunogenic epitope" and the definitions provided in the instant Specification. See instant Specification "a nucleic acid sequence selected from (page 7, lines 7-8)"; "selecting at least a portion of the codons encoding HC from codons preferred from expression in a host organism (page 7, lines 29-31)"; "fragments of the botulinum neurotoxin protein expressed by recombinant organisms. Specifically peptides comprising protective epitopes from the receptor binding domain(see page 11, lines 23-24); "The vaccine comprises fragments of the A and B toxins (page 11, lines 31-32)"; to include peptide epitopes and not the complete amino acid sequence of SEQ Id NO 4, wherein the claims are directed to a nucleic acid that encodes at least one epitope. The alignment provided is not commensurate in scope with the instantly claimed invention. The rejection could be obviated by amending the claims to no longer recite [at least one epitope] and just to recite " comprises... SEQ ID NO 3."

LaPenotiere et al still anticipates the instantly claimed invention as now claimed and for reasons of record in light of evidence provided by Atassi et al (1999, Structure, activity and immune (T and B cell), pages 248-249) and Clayton et al (June 1995, reference of record) title, and page 2739, Figure 1) that show the nucleic acid of LaPenotiere et al (see abstract, page 465, paragraph 2 "inclusion bodies", "E.coli lystate") to encode at least one epitope held in common with SEQ ID NO 4, and is a nucleic acid that comprises a nucleic acid sequence of SEQ ID NO 3, the encoded amino acid sequence comprising at least one immunogenic epitope of the Hc domain of Clostridium botulinum toxin Type A. The alignment provided is not commensurate in scope with the instantly claimed invention. The rejection could be obviated by amending the claims to no longer recite [at least one epitope].

9. ***Claim Rejections - 35 USC § 102, Rejection Maintained)*** The rejection of claims 42-45, 48, 50, 82 rejected under 35 U.S.C. 102(b) as being anticipated by Thompson et al (1990) is traversed on the same grounds as that set forth above for LaPenotiere et al.

10. It is the position of the examiner that Thompson et al still inherently anticipates the instantly claimed invention for the same reasons set forth above for LaPenotiere et al (responses incorporated herein by reference), wherein the claims recite the phrase "comprising at least one immunogenic epitope" and the nucleic acid sequence of Thompson et al encodes an amino acid sequence that comprises at least one immunogenic epitope of SEQ ID NO 4.

New Combination of Claim Limitations/New Grounds of Objection/Rejection

Claim Objections

11. Claims 43, 55 and 56 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

12. Claim 43 has been amended to depend from claim 87. Claim 87 is directed to "An isolated or purified nucleic acid comprising the nucleic acid of SEQ ID NO:3." Claim 43 is directed to a fragment range of the sequence set forth in SEQ ID NO :3 and therefore is broader is scope than claim 87, the claim from which claim 43 depends. The fragment range of nucleic acids of 13-1314 of SEQ ID NO 3 claimed in amended claim 43, is smaller in size than SEQ ID NO 3, and may comprise any number of additional nucleic acids and is not required to evidence

the structural components of the nucleotides of positions 1-12 of SEQ ID NO 3 and therefore sets forth a broader genus of nucleic acids than that claimed in independent claim 87.

12. Claims 55 and 56 have been amended to depend from claim 87 which recites SEQ ID NO 3, which is a specific nucleic acid sequence, and claims 55 and 56 seek to change the nucleic acid sequence set forth in claim 87 by changing the overall AT content of the total base composition from that which is set forth in claim 87. Therefore, claims 55 and 56 broaden the scope of claim 87 from which they depend and are not further limiting of independent claim 87.

13. Amended claims 48-49, 53, and new claims 88-89, 90-92 are objected to for reciting the term "mammalian cell"; the instant specification defines only mammalian cell lines in a method of preparing a polypeptide. The claims should be amended to be consistent with the disclosure in the instant Specification.

14. Amended Claims 43-47, 55-56, 49-51 are objected to because of the following informalities: Claims 43-47, 55-56, and 49-51 depend directly or indirectly from a later appearing claims. Claims should depend from a prior claim. Appropriate correction is required.

Claim Rejections - 35 USC § 101

15. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

16. Amended claims 48-49, 53, 82 and new claims 88-89, 90-92 are directed to non-statutory subject matter. Amended claims 48-49, 53, 82 (depends from amended claim 45) and new claims 88-89, 90-92 recite the term "mammalian cell " which reads on cells present in a transfected mammal, which would include transfected humans. Claiming transfected humans is a non-statutory category of invention.

Claim Rejections - 35 USC § 102

18. Claims 42, amended claims 48-49, 53, 51, 55 (amended and depends from claim 42) and 56 (amended and depends from claim 42), amended claims 85-86 and new claims 88-89, 90-92 are rejected under 35 U.S.C. 102(b) as being anticipated by Romanos et al (1991, reference on Applicant's USPTO 1449) as evidenced by Atassi et al (1999).

(Instant claim 42, 48-49, 53, 88-89, 90-92) Romanos et al disclose the instantly claimed invention directed to an isolated nucleic acid (gene synthesis, title, page 1461) encoding at least one epitope of SEQ ID NO 4 (see evidence provided by Atassi et al, pages 248 and 249, Figure 14 and Table 5 which evidence shows Te (tetanus toxin) and botulinum toxin type A, heavy chain C-fragments comprise an amino acid sequence of SEQ ID NO 4), wherein tetanus toxin shares conserved amino acid sequences that are also inherently immunogenic (see Atassi et al, Table 5, page 249 provides evidence that the conserved amino acids comprise at least one epitope) with SEQ ID NO 4.

(Instant claims 44-46) The nucleic acid of Romanos et al evidenced an overall AT content of about 63% and a GC content of about 47% (see Romanos et al, page 1465, col. 2, paragraph 2).

(Instant claims 51, 85-86) A recombinant host cell disclosed included Pichia pastoris (see page 1466, col. 1, last paragraph) and the level of expression of the recombinant nucleic acid resulted in the recombinant fragment C that comprises at least one immunogenic epitope of SEQ ID 4, was to levels of over 25% of the total cell protein.

Romanos et al inherently anticipates the instantly claimed invention as now claimed in light of evidence provided by Atassi et al showing tetanus toxin and botulinum toxin type A to share conserved immunogenic amino acid epitopes within the heavy chain fragment-C domain, the amino acids being an amino acid sequence of SEQ ID NO 4.

Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
October 11, 2005

L. R. F. Smith

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